510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K200801

B Applicant

Immunalysis Corporation

C Proprietary and Established Names

Quantisal™ Oral Fluid Collection Device

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PJD	Class II	21 CFR 862.1675 - Blood Specimen Collection Device	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Not applicable.

C Type of Test:

Collection, preservation and transport of oral fluid specimens for drugs of abuse testing for tetrahydrocannabinol (THC), cocaine and its metabolite benzoylecgonine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, benzodiazepines and tramadol.

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

For In Vitro Diagnostic Use

The Quantisal Oral Fluid Collection Device is intended for the collection, preservation and transport of oral fluid specimens for tetrahydrocannabinol (THC), cocaine and its metabolite benzoylecgonine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, benzodiazepines and tramadol.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

The Quantisal™ Oral Fluid Collection Device is intended for the collection, preservation and transport of oral fluid specimens for tetrahydrocannabinol (THC), cocaine and its metabolite benzoylecgonine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, benzodiazepines and tramadol. The device consists of a single cellulose pad affixed to a polypropylene stem. The oral fluid sample is collected by placing the cellulose pad under the tongue.

B Principle of Operation:

An oral fluid specimen is collected by placing the collector under the tongue of an individual until a defined volume of saliva has saturated the cellulose pad. The defined volume taken up by the cellulose pad is indicated by coloration (blue) in a window on the stem (the volume adequacy indicator). The collector is then transferred into a provided polypropylene tube containing a specific volume of preservative buffer, and stoppered with the provided cap. The specimen is then ready for storage or transport.

The Quantisal™ Oral Fluid Collection System collects 1 mL of neat oral fluid and dilutes it with 3 mL of preservative buffer. This results in a X4 dilution factor.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Quantisal II Oral Fluid Collection Device

B Predicate 510(k) Number(s):
K183048

C Comparison with Predicate(s):

Device & Predicate Device(s):	K200801	K183048
Device Trade Name	Quantisal™ Oral Fluid Collection Device	Quantisal II Oral Fluid Collection Device
General Device Characteristic Similarities		
Intended Use/Indications For Use	Same	Collection, preservation and transport of oral fluid specimens for tetrahydrocannabinol (THC), cocaine and its metabolite benzoylecgonine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, benzodiazepines and tramadol
Sample Matrix	Same	Human oral fluid only
Components	Same	Cellulose pad, polypropylene stem and transport tube
Sample Collection	Same	A cellulose pad is placed under the tongue for collection until blue dye visible in the window of the stem
Transport Tube	Same	Polypropylene tube containing preservative buffer
General Device Characteristic Differences		
Collector	Collector containing one pad	Collector containing two pads. These two pads can be separated after collection
Sample Volume	1 mL	1 mL on each pad, 2 mL in total
No. of Transport Tubes	1 transport tube	2 transport tubes, 1 for each pad

VI Standards/Guidance Documents Referenced:

- ISO 14971:2007 Medical Devices – Application of Risk Management to Medical Devices
- EN ISO 14971:2012 Medical Devices – Application of Risk Management to Medical Devices

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Not applicable.

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Assay Reportable Range:

   Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Sample Volume

   The sponsor performed a study to evaluate the consistency of the oral fluid sample volume collected by the Quantisal™ Oral Fluid Collection device. In this study, seventy-five oral fluid samples from known drug users were collected using the device.

   After the volume adequacy indicator turned blue on the collector stems, the collector was weighed and compared to the average weight of collector before collection. The difference in weight was noted, and the volume was calculated using the weight difference and the specific gravity for saliva based on scientific literature references. Summary results of the study were as follows:

Mean (mL)	1.003
SD (mL)	0.040
CV%	4.017
Min (mL)	0.935
Max (mL)	1.081

Sample Collection Time

The sponsor performed a study to evaluate the range of collection times observed in which seventy-five oral fluid samples from known drug users were collected using Quantisal™ Oral Fluid Collection device. A timer was started at the time the collector was placed into subject's mouth and stopped when the volume adequacy indicator turned blue on collector stem and the collector was taken out of the mouth. The length of time was documented.

The results demonstrated that all of the subjects were able to provide an adequate volume of oral fluid within 10 minutes using the Quantisal device. The mean time required for collection was 3 minutes and 51 seconds. The maximum time required for collection was 7 minutes 0 seconds.

Drug Recovery

The sponsor performed a study to evaluate the analytical recovery of drugs from oral fluid samples collected with the Quantisal™ Oral Fluid Collection Device. The samples under test for each drug (THC, benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, nordiazepam, and tramadol) were prepared by spiking the drug into negative oral fluid at ±25% and +50% of the cutoff concentration used, resulting in the target concentrations listed in the table below.

None of the test samples were provided directly from human donors. The sample preparation (spiking) was done in borosilicate glass tubes.

Three Quantisal™ Oral Fluid Collection Devices were then introduced sequentially into each aliquot and removed after the volume adequacy indicator turned blue. The collector was then placed into the transport tube, sealed with a snap cap and stored overnight at room temperature. The next day the pad was separated from the stem and the liquid in the tube was analyzed by GC-MS or LC-MS-MS in replicates of three to determine percentage recovery. The results of the study are summarized in the table below.

Drugs	Target Concentration (ng/mL)	Mean recovery (%)	Low recovery (%)	High recovery (%)
THC	3	93.83	90.26	99.57
	5	97.20	92.71	106.04
	6	94.81	91.15	100.58
Benzoylecgonine	11.25	98.5	91.18	104.06
	18.75	97.16	90.64	108.72
	22.5	101.23	92.97	109.01
Cocaine	11.25	92.06	90.86	92.97
	18.75	97.40	91.26	108.95
	22.5	98.63	91.15	108.85
Morphine	22.5	95.12	92.24	99.71
	37.5	95.89	92.91	97.89
	45	100.34	90.77	109.36

Drugs	Target Concentration (ng/mL)	Mean recovery (%)	Low recovery (%)	High recovery (%)
Codeine	22.5	94.68	90.42	101.74
	37.5	98.42	90.45	109.53
	45	99.11	90.13	109.39
Oxycodone	22.5	95.10	90.74	102.05
	37.5	97.74	90.67	109.56
	45	99.13	90.29	109.38
Hydrocodone	22.5	100.09	91.48	109.36
	37.5	101.16	91.11	108.78
	45	101.35	90.05	108.54
6-acetylmorphine	3	93.91	91.87	95.99
	5	97.12	91.35	107.2
	6	94.22	90.39	106.82
Phencyclidine	7.5	94.55	90.45	99.36
	12.5	97.57	91.87	107.2
	15	95.78	90.48	100.64
Amphetamine	37.5	98.67	97.58	100.25
	62.5	93.27	91.52	95.56
	75	94.28	92.46	96.49
Methamphetamine	37.5	94.07	92.38	97.75
	62.5	91.95	90.38	93.42
	75	93.03	91.27	95.39
Buprenorphine	2.25	99.95	90.65	103.6
	3.75	102.98	90.03	106.68
	4.5	97.87	94.25	101.4
Methadone	15	95.04	93.2	98.62
	25	93.68	90.24	98.5
	30	93.85	92.14	95.74
Benzodiazepines	3.75	103.64	98.61	107.98
	6.25	105.72	101.63	107.69
	7.5	96.39	94.74	96.97
Tramadol	37.5	96.08	90.43	101.86
	62.5	99.15	90.57	108.93
	75	92.40	90.43	96.93

All recoveries for all drugs at all concentrations were within ± 10% of the reference measurement.

The sponsor performed studies to evaluate the extraction efficiency of human oral fluid out of the Quantisal collection pad and into the transport buffer solution, and separately to evaluate the stability of the drugs in the diluted oral fluid samples stored in the Quantisal transport tube at 25^{o}C and at 2^{o} – 8^{o} C.

All test samples for these studies were prepared by spiking into pools of drug-free oral fluid at a concentration +50% of the cutoff. The sample preparation (spiking) was done in borosilicate glass tubes. None of the test samples were provided directly from human donors.

Oral Fluid Sample Extraction Efficiency

The concentration of each spiked sample solution pool was confirmed by GC-MS or LC-MS/MS in replicates of three to establish the initial concentration. Samples were then collected by dipping the collection pad into the spiked sample and stored in three independent Quantisal™ Oral Fluid Collection Devices. GC-MS or LC-MS/MS testing was performed in three replicates for each device at each of the following time points:

- immediately after being placed into the collection tube.
- at 4 hours, 24 hours, 5 days, and 10 days post collection at 25°C
- at 5 days, 10 days, and 1, 2, and 3 months post collection at 2°C - 8°C

At each time point, aliquots from each of the three collection devices were analyzed in triplicate, for a total of nine measurements per concentration per drug.

After insertion of the Quantisal collector pad into the transport tube, the neat oral fluid containing drug extracts into the buffer solution over a period of time. Extraction efficiency of drug into solution was evaluated during the first 24 hours post-collection to determine the point at which extraction was complete. The device is intended for transport of oral fluid samples to a laboratory for drug testing after the sample is collected (typically overnight and estimated to be 8-24 hours), and immediate use of the diluted sample is not expected or recommended. The labeling for the device states that samples should not be tested until a minimum of 4 hours has passed after specimen collection to allow sufficient time for any drug(s) present to be extracted from the pad into the preservation buffer.

Extraction efficiency in terms of percent drug recovery was calculated at the immediate, 4-hour, and 24-hour time points (under ambient room temperature storage) by comparing the average concentration of the nine replicates to the initial concentration of the spiked oral fluid pool before collection by the Quantisal device. At 24 hours, the recoveries for all drugs ranged from 93% to 102%, and this timepoint was used as the baseline comparison for evaluating sample stability at the remaining timepoints in the study.

The reason for using the timepoint of 24 hours instead of the immediate timepoint was to ensure that sample extraction was not confounding the sample stability results.

Oral Fluid Sample Stability After Extraction

Sample stability in terms of % of initial concentration was calculated at Day 5 and Day 10 time points at ambient temperature (25^{o} C) and Day 5, Day 10, Month 1, Month 2 and Month 3 time points at 2 – 8^{o} C by comparing each timepoint to the concentration at 24 hours.

All analytes were considered to be stable up to 10 days at room temperature (up to 25°C) and up to 3 months at 2 - 8 °C) except for THC and cocaine.

THC is stable for up to 10 days at room temperature and up 2 months at 2 - 8 °C.

Cocaine is stable for up to 5 days at room temperature and up 1 month stored at 2 - 8 °C. Cocaine is unstable in samples and converts to benzoylecgonine. Benzoylecgonine is the metabolite of cocaine and is found only in samples from subjects who have taken cocaine.

Recoveries were as follows:

At 25ºC

Analyte	Concentration (ng/mL)		
	24 hours	Day 5	Day 10
THC	6.0	5.9	5.9
Benzoylecgonine	22	23	23
Cocaine	22	22	14
Morphine	45	45	43
Codeine	46	44	45
Oxycodone	47	45	45
Hydrocodone	46	45	45
6-acetylmorphine	5.8	6.0	5.9
Phencyclidine	14	14	15
Amphetamine	75	75	74
Methamphetamine	74	76	75
Buprenorphine	4.5	4.7	4.5
Methadone	29	28	29
Benzodiazepines	7.5	7.5	7.5
Tramadol	75	75	75

At 2-8ºC

Analyte	Concentration (ng/mL)					
	24 hours	Day 5	Day 10	Month 1	Month 2	Month 3
THC	6.0	6.0	6.0	5.3	5.4	5.1
Benzoylecgonine	22	23	22	22	22	21
Cocaine	22	21	20	22	18	17
Morphine	45	45	44	46	45	45
Codeine	46	44	44	45	44	44
Oxycodone	47	46	45	46	44	45
Hydrocodone	46	45	44	45	45	43
6-acetylmorphine	5.8	6.1	6.0	6.0	5.9	5.9
Phencyclidine	14	14	14	15	14	14
Amphetamine	75	74	74	73	74	75
Methamphetamine	74	76	73	75	72	75
Buprenorphine	4.5	4.6	4.4	4.5	4.5	4.6
Methadone	29	28	30	29	28	28
Benzodiazepines	7.5	7.4	7.5	7.7	7.8	7.3
Tramadol	75	75	73	76	76	75

Based upon these results, the sponsor makes the following stability claims:

Analyte	Stability at 8-25°C	Stability at 2-8°C
THC	10 days	2 months
Benzoylecgonine	10 days	3 months
Cocaine	5 days	1 month
Morphine	10 days	3 months
Codeine	10 days	3 months
Oxycodone	10 days	3 months
Hydrocodone	10 days	3 months
6-acetylmorphine	10 days	3 months
Phencyclidine	10 days	3 months
Amphetamine	10 days	3 months
Methamphetamine	10 days	3 months
Buprenorphine	10 days	3 months
Methadone	10 days	3 months
Benzodiazepines	10 days	3 months
Tramadol	10 days	3 months

Borosilicate Glass Vial Stability

The sponsor performed a study to evaluate whether borosilicate glass vials used for collection of expectorated neat oral fluid sample could affect the drug concentrations.

All test samples for this study were prepared by spiking into drug-free oral fluid. None of the test samples were provided directly from human donors.

Drug free expectorated oral fluid was spiked with the drug analyte at a concentration +50% of the respective cutoffs. The initial concentration of the solution was analyzed by GC-MS or LC-MS-MS. Three borosilicate glass vials were introduced sequentially into each aliquot, stored at 25°C for 48 hours, and then tested using the same analytical method in replicates of three for each vial.

The mean variation in % recovery for each analyte was as follows:

Drugs	% recovery
THC	93.5
Benzoylecgonine	100.9
Cocaine	99.4
Morphine	93.4
Codeine	100.6
Oxycodone	95.5

Drugs	% recovery
Hydrocodone	97.2
6-acetylmorphine	100.8
Phencyclidine	99.5
Amphetamine	98.7
Methamphetamine	99.0
Buprenorphine	100.0
Methadone	104.2
Benzodiazepines	100.3
Tramadol	99.4

Sample Transportation Stability

The sponsor performed a study to evaluate the stability of drugs in human oral fluid samples during transportation. All test samples for this study were prepared by spiking into drug-free oral fluid. None of the test samples were provided directly from human donors.

Drug free oral fluid was spiked with the drug analyte at a concentration ± 50% of the screening cutoffs. Three Quantisal™ Oral Fluid Collection Devices were introduced sequentially into each aliquot and removed after the volume adequacy indicator turned blue. The collector of each Quantisal was then placed into the transport tube, sealed with a snap cap and packed in standard boxes used by carriers. During the 4-day (96 hours) simulated transportation study, the samples were stored in an oven or freezer at temperatures ranging from -20°C – 40°C following the transport simulation design below to encompass the temperatures likely to occur during shipment of products. The device used as the reference (unstressed) condition was stored continuously at the recommended storage condition at 2°C - 8°C.

The temperatures and duration at each step and temperature were as follows:

Step	Cycle Temperature (°C)	Duration (hour)
1	-20±5	1
2	4±5	1
3	15±5	63
4	25±5	27
5	30±2	2
6	35±2	1
7	40±2	1

After proceeding sequentially through all seven temperature conditions, the samples were analyzed using LC-MS/MS in replicates of two for each sample and compared to the reference sample. The % recoveries for individual replicates were all within ± 10% of the samples stored at the recommended condition of 2°C - 8°C.

Supplemental Sample Transportation Stability

The sponsor also provided a supplemental sample transportation stability study to further verify the stability of the drug analyte in human oral fluid samples collected by the Quantisal device during transportation, including exposure to extreme temperatures for up to 24 hours.

All test samples for this study were prepared by spiking into drug-free oral fluid. None of the test samples were provided directly from human donors.

Drug free oral fluid was spiked with the drug analyte at a concentration ± 50% of the screening cutoffs. Nine Quantisal™ Oral Fluid Collection Devices were introduced sequentially into each aliquot and removed after the volume adequacy indicator turned blue. The collector was then placed into the transport tube, sealed with a snap cap and packed in standard boxes used by common carrier (FedEx). Three each of the Quantisal transport tubes containing specimen (per each concentration) were stored at 25°C (room temperature) for 24 hours to simulate uncontrolled ambient conditions, and a second set (three each per concentration) of transport tubes were stored at 40°C for 24 hours to simulate extreme heat conditions. The third set of tubes (three each per concentration) was used as the reference (unstressed) condition and was stored continuously at the recommended storage condition at 2°C - 8°C. Each of the tubes was agitated using a platform rocker for 6 hours during the 24-hour simulation. LC-MS/MS testing was performed in replicates of two for each transport tube sample and compared to the reference sample.

The % recoveries for individual replicates at 25° C and 40° C were all within ± 10% of the samples stored at the recommended condition of 2°C - 8°C.

Clinical Specimens Testing

Expectorated Oral Fluid Samples Processed Through Quantisal (Dipping Study)

The sponsor performed a study to evaluate whether drug concentrations in native unaltered samples collected by the Quantisal device are comparable to the expectorated neat oral fluid concentrations.

Sixty de-identified, unaltered oral fluid samples containing drug for each drug class were collected from self-reported drug users by expectoration (spitting) and shipped to Immunalysis overnight. A minimum of ten samples of each drug were within ± 50% of the cutoffs. The expectorated samples were analyzed at the laboratory by LC-MS/MS or GC-MS. A Quantisal device was introduced into each expectorated sample and removed after the volume adequacy indicator turned blue. The time until the volume adequacy indicator turned blue was noted. The collector was then placed into the transport tube, sealed with a snap cap and stored overnight at room temperature. The next day the pad was separated from the stem and the liquid in the tube was analyzed by mass spectrometry. The Quantisal results were compared to expectorated results and the range of recoveries and the linear regression statistics for each analyte is presented below:

Analyte	Slope	Intercept	R^2
THC	0.982	0.87	0.99
Benzoylecgonine	0.843	3.54	0.98
Cocaine	0.891	3.50	0.99
Morphine	0.961	-1.54	0.99
Codeine	0.955	-1.05	0.99
Oxycodone	0.969	-1.25	1.00
Hydrocodone	0.922	-1.13	0.99
6-acetylmorphine	0.986	-0.75	0.99
Phencyclidine	0.979	-0.41	1.00
Amphetamine	0.906	1.30	0.99
Methamphetamine	0.941	-0.44	0.99
Buprenorphine	0.889	1.02	0.99
Methadone	0.997	-0.20	1.00
Benzodiazepines	0.946	-0.04	0.99
Tramadol	0.936	0.07	0.99

Biocompatibility

The Quantisal Device has short term contact with the patient's mouth during oral fluid collection. The sponsor provided information on biocompatibility and cytotoxicity which was reviewed and found to be acceptable.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable.

2. Matrix Comparison:

   Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.